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CLAIMS:

1. A combination of substances, at least two of which exhibit amphipatic properties when contacted with a suitable liquid medium, said two substances differing  
5 in their solubility in this medium and said combination being capable of forming extended surfaces, especially membrane surfaces, in contact with said medium, such that molecules of an amphipatic third substance can associate with said surface, wherein said at least two substances are selected so that
- substance which is more soluble in said liquid medium than the other substance forms  
10 less extended surfaces than said other substance of the combination and
  - molecules of the third substance are more likely to associate with the extended surfaces formed by the other at least two substances combined than with an extended surface formed by said other, less soluble substance alone.
- 15 2. A combination of substances, at least two of which exhibit amphipatic properties when contacted with a suitable liquid medium, said two substances being capable of forming, at least when combined, an extended surface, especially a membrane surface, in contact with said medium, said surface carrying a net electric charge, such that molecules of a further amphipatic substance with a net electric charge  
20 can associate with said surface, and the net charge density of the surface and the net charge of the amphipatic molecules associating with the surface have the same sign (both negative or both positive).
3. A combination of substances, at least two of which exhibit amphipatic  
25 properties when contacted with a suitable liquid medium said two substances differing in their solubility in this medium and being capable of forming, at least when combined, extended surfaces, especially membrane surfaces, in contact with said medium, such that molecules of an amphipatic third substance can associate with said surfaces, said at least two substances being selected so that
- 30 -the substance which is more soluble in said liquid medium than the other substance forms less extended surfaces than said other substance of the combination,

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-the surfaces formed by the combined substances as well as the molecules of the third substance likely to associate with said surface, are both negatively charged or both positively charged.

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5. A combination according to ~~claims 1, 2 or 3;~~  
**characterised in that** it comprises at least one amphipathic substance capable of self-aggregating to form an extended surface, and at least one amphipathic substance which, when incorporated into said surface, supports an increased curvature of said surface, the concentration of said curvature-increasing substance being below 99% of the saturation concentration, or of that concentration above which the surface could not be formed, whichever is higher.

6. A combination according to claim 4 ~~or 5~~,  
**characterised in that** the concentration of said more soluble or curvature-increasing substance amounts to at least 0.1 %, frequently to 1-80 %, more preferably to 10-60 %, and most preferably to 20-50 % of the relative concentration as defined in claim 5.

7. A combination according to claim 5 ~~or 6~~,  
**characterised in that** the surfaces have an average curvature (defined as the inverse  
average radius of the areas enclosed by the surfaces) corresponding to an average radius

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5 **characterised in that** the surface is supported by a solid, especially by a supporting surface of suitable curvature or size

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Claim 2  
one of claims 2 through

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*do*

Claim 2

characterised in that the substance which is less soluble in the liquid medium, and which preferably is the surface-building and/or charge carrying amphipatic substance in the system, is a lipid or lipid-like material, whereas the substance which is more soluble in the liquid medium, and preferably is the substance causing increased surface curvature, flexibility or adaptability and/or is the charge carrying substance, is a surfactant, or is identical with the third, associating substance.

62 *claim 1*13. The combination of ~~any one of claims 1 through 12,~~

**characterised in that** it comprises arrangements of molecules in the form of minute fluid droplets suspended or dispersed in a liquid medium and surrounded by a membrane-like coating of one or several layers of at least two kinds or forms of self-aggregating amphiphilic substances, said at least two substances having an at least 10-fold, preferably an at least 100-fold difference in solubility in the preferably aqueous, liquid medium, such that the average diameter of homo-aggregates of the more soluble substance or of hetero-aggregates of both substances is smaller than the average diameter of homo-aggregates of the less soluble substance.

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*claim 1*

14. Combination according to ~~any one of the preceding claims,~~ wherein the total content of all amphipats that can form a surface is between 0.01 and 30 weight-%, particularly between 0.1 and 15 weight-%, and most preferably between 1 and 10 weight-% of the total dry mass of the aggregates, especially if the combination is to be

15 applied on or in the human or animal body.

*claim 1*15. Combination according to ~~any one of the preceding claims,~~

**characterised in that** it contains at least one (bio)compatible polar or non-polar surface-supporting lipid as the substance which forms more extended surfaces, wherein the surfaces formed by the combination preferably have a bilayer structure.

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16. Combination according to claim 15, wherein said extended surface-forming substance is a lipid or a lipoid from a biological source or a corresponding synthetic lipid, or is a modification of such a lipid, preferably a glyceride,

25 glycerophospholipid; isoprenoidlipid, sphingolipid, steroid, sterine or sterol, a sulphur- or carbohydrate-containing lipid, or any other lipid capable of forming bilayers, in particular a half-protonated fluid fatty acid, and preferably selected from phosphatidylcholines, phosphatidylethanolamines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids, phosphatidylserines, sphingomyelins or  
30 sphingophospholipids, glycosphingolipids (e.g. it is a cerebroside, ceramidpolyhexoside, sulphatide, sphingoplasmalogene), gangliosides, or other glycolipids or synthetic lipids, in particular of the dioleoyl-, dilinoleyl-, dilinolenyl-,

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Clavin 12

17. Combination according to any of claims 12 through 16, wherein said surfactant is a nonionic, a zwitterionic, an anionic or a cationic surfactant, especially a long-chain fatty acid or alcohol, an alkyl-tri/di/methyl-ammonium salt, an alkylsulphate salt, a monovalent salt of cholate, deoxycholate, glycocholate, glycodeoxycholate, taurodeoxycholate, or taurocholate, an acyl- or alkanoyl-dimethyl-aminoxide, esp. a dodecyl- dimethyl-aminoxide, an alkyl- or alkanoyl-N-methylglucamide, N-alkyl-N,N-dimethylglycine, 3-(acyldimethylammonio)-alkanesulphonate, N-acyl-sulphobetaine, a polyethylen-glycol-octylphenyl ether, esp. a nonaethylen-glycol-octylphenyl ether, a polyethylene-acyl ether, esp. a nonaethylen-dodecyl ether, a polyethyleneglycol-isoacyl ether, esp. a octaethyleneglycol-isotridecyl ether, polyethylene-acyl ether, esp. octaethylenedodecyl ether, polyethyleneglycol-sorbitane-acyl ester, such as polyethylenglykol-20-monolaurate (Tween 20) or polyethylenglykol-20-sorbitan-monooleate (Tween 80), a polyhydroxyethylene-acyl ether, esp. polyhydroxyethylene-lauryl, -myristoyl, -cetylstearyl, or -oleoyl ether, as in polyhydroxyethylen-4 or 6 or 8 or 10 or 12, etc. -lauryl ether (as in Brij series), or in the corresponding ester, e.g. of polyhydroxyethylen-8-stearate (Myrj 45), -laurate or -oleate type, or in polyethoxylated castor oil 40 (Cremophor EL), a sorbitane-monoalkylate (e.g. in Arlacel or Span), esp. sorbitane-monolaurate (Arlacel 20, Span 20), an acyl- or alkanoyl-N-methylglucamide, esp. in or decanoyl- or dodecanoyl-N-methylglucamide, an alkyl-sulphate (salt), e.g. in lauryl- or oleoyl-sulphate, sodium deoxycholate, sodium glycodeoxycholate, sodium oleate, sodium taurate, a fatty acid salt, such as sodium elaidate, sodium linoleate, sodium laurate, a lysophospholipid, such as n-octadecylene(=oleoyl)-glycerophosphatidic acid, -phosphorylglycerol, or -phosphorylserine, n-acyl-, e.g. lauryl or oleoyl-glycero-phosphatidic acid, -phosphorylglycerol, or -phosphorylserine, n-tetradecyl- glycero-phosphatidic acid, -phosphorylglycerol, or -phosphorylserine, a corresponding palmitoeloyl-, elaidoyl-, vaccenyl-lysophospholipid or a corresponding short-chain phospholipid, or else a surface-active polypeptide.

64 Claim 12

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Claim 11

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**characterised in that** the third substance is of biological origin, and preferably is bioactive.

65 *Claim 1*  
23. Combination according to ~~any one of claims 1 through 22,~~

**characterised in that** the third substance associates with the membrane-like extended surface, especially by inserting itself in the interface(s) between the membrane and the liquid medium in contact with said membrane.

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*Claim 1*  
24. Combination according to ~~any one of claims 1 to 23,~~ wherein the content

of chain molecules corresponding to said third substance, is between 0.001 and 50 rel.

% compared to the mass of adsorbent surface and often is between 0.1 and 35 rel. %, more preferably is between 0.5 and 25 rel. %, and most suitably is between 1 and 20

10 rel. %, whereby the specific ratio value is likely to decrease with increasing molar mass of said chain molecules.

*Claim 21*  
25. Combination according to ~~any one of claims 21 through 24,~~ wherein

chain molecule is a protein, and at least a part of said molecule is associated with the

15 surface, provided that such part has at least three segments or functional groups with a propensity to bind to said surface.

*Claim 21*  
26. Combination according to ~~any one of claims 21 through 24,~~

**characterised in that** said chain molecules belong to the class of polynucleotides, such

20 as DNA or RNA, in the natural form or after chemical, biochemical, or genetic modification.

*Claim 21*  
27. Combination according to ~~any one of claims 21 through 24,~~

**characterised in that** said chain molecules belong to the class of polysaccharides with

25 at least partial propensity to interact with the surface either in the natural form or after some chemical, biochemical, or genetic modification.

*Claim 21*  
28. Combination according to ~~any one of claims 21 through 27,~~ wherein the

chain molecule can act as an adrenocorticostaticum, a  $\beta$ -adrenolyticum, an androgen or

30 antiandrogen, antiparasiticum, anabolicum, anaestheticum or analgesicum, analepticum, antiallergicum, antiarrhythmicum, antiarteroscleroticum, antiasthmaticum and/or bronchospasmolyticum, antibioticum, antidrepressivum and/or antipsychoticum,

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31. Combination according to ~~any one of the preceding claims~~, wherein said third substance agent is an enzyme, a co-enzyme or some other kind of bio-catalyst.

67 *Claim 1*

32. Combination according to ~~any one of the preceding claims~~, wherein said third substance agent is a recognition molecule, including inter alia adherins, antibodies, catenins, selectins, chaperones, or parts thereof.

*Claim 1*

5 33. Combination according to ~~any one of the preceding claims~~, wherein said agent is a hormone, especially insulin.

*Claim 1*

34. Combination according to ~~any one of the preceding claims~~,  
**characterised in that** it contains 1 through to 500 I.U. insulin/mL, in particular  
10 between 20 and 400 I.U. insulin/mL and most preferred between 50 and 250 I.U. insulin/mL, preferably of human recombinant or humanised type.

*Claim 1*

35. Combination according to ~~any one of the preceding claims~~,  
**characterised in that** it contains between 0.01 mg and 20 mg interleukin/mL, in  
15 particular between 0.1 and 15 mg and most preferred between 1 and 10 mg interleukin/mL, said interleukin being suitable for the use in humans or animals, including IL-2, IL-4, IL-8, IL-10, IL-12, if necessary after a final dilution to reach the practically desirable drug concentration range.

*Claim 1*

20 36. Combination according to ~~any one of the preceding claims~~,  
**characterised in that** it contains up to 20 relative wt-% interferon, in particular between 0.1 and 15 mg interferon/mL and most preferred between 1 and 10 mg interferon/mL, said IF being suitable for the use in humans or animals, including but not  
25 restricted to IF alpha, beta and gamma, can be used, if necessary after a final dilution that brings the drug concentration into practically preferred concentration range.

*Claim 1*

37. Combination according to ~~any one of the preceding claims~~,  
**characterised in that** it contains up to 25 mg nerve growth factor (NGF) / mL suspension or up to 25 relative w-% of NGF as an agent, especially 0.1-15 rel. w-%  
30 protein and most preferred between 1 and 10 rel. wt-% NGF, preferably human recombinant NGF and, if needed, diluted before use.

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68 Claim

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claim 39

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25                    46.     The method of claim 45,  
                       **characterised in that** at least one edge-active substance or a surfactant, at least one  
                       amphiphilic substance, at least one hydrophilic fluid and the agent are separately mixed  
                       and, if required, dissolved to form a solution, the resulting mixtures or solutions then  
                       being combined to subsequently induce, preferably by action of mechanical energy, the  
 30                    formation of the entities which associate with the agent molecules.

~~pages 45 or 46~~

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claim 45

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Claim 45

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*claim 1*  
53. Use of a combination of substances in accordance with ~~any one of the~~  
~~preceding claims~~, for the preparation of drug carriers, drug depots, or for any other kind  
of medicinal or biological application.

5           54     Use of a combination of substances in accordance with ~~any one of the~~  
~~preceding claims~~, in bioengineering or for genetic manipulations. *claim 1*

*claim 1*  
55. Use of a combination of substances in accordance with ~~any one of the~~  
~~preceding claims~~, in separation technology, for (bio)processing or for diagnostic  
10   purposes.

*claim 1*  
56. Use of a combination of substances in accordance with ~~any one of the~~  
~~preceding claims~~ to stabilise surface-associating molecules, especially chain molecules,  
that are at least partially amphipatic, such as (derivatised) proteins, polypeptides,  
15   polynucleotides, or polysaccharides and/or in catalysing processes which involve such  
molecules in the surface-associated state.

*claim 1*  
57. Use of a combination of substances in accordance with ~~any one of the~~  
~~preceding claims~~ to affect the kinetics and/or the reversibility of association or  
20   dissociation between said surface-associating molecules and a complex, adaptable  
surface, whereby the higher surface charge density and/or greater surface softness and/or  
surface defect density speeds up the association, or the corresponding reduction slows  
down the rate of association or else induces partial molecular dissociation.

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add B<sup>3</sup>

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